Calculate the difference between the potency and the amoxicillin content as follows:

$$\text{Difference} = \frac{\dfrac{\text{Potency in micrograms}}{\text{per milligram}}}{10} - \begin{array}{l}\text{percent} \\ \text{amoxicillin} \\ \text{content}\end{array}$$

(ii) *Base titration.*

$$\text{Percent amoxicillin content} = \frac{\dfrac{(A-B)(\text{normality of perchloric acid reagent})}{(365.4)(100)(100)}}{(\text{Weight of sample in milligrams})(100-m)}$$

where:
  A=Milliliters of perchloric acid reagent used in titrating the sample.
  B=Milliliters of perchloric acid reagent used in titrating the blank.
  *m*=Percent moisture content of the sample.

Calculate the difference between the potency and the amoxicillin content as follows:

$$\text{Difference} = \frac{\dfrac{\text{Potency in micrograms}}{\text{per milligram}}}{10} - \begin{array}{l}\text{percent} \\ \text{amoxicillin} \\ \text{content}\end{array}$$

(6) *Crystallinity.* Proceed as directed in §436.203(a) of this chapter.

(7) *Identity.* Proceed as directed in §436.211 of this chapter, using a 0.5 percent potassium bromide disc prepared as described in paragraph (b)(1) of that section.

[39 FR 34032, Sept. 23, 1974, as amended at 46 FR 16682, Mar. 13, 1981; 49 FR 3458, Jan. 27, 1984; 50 FR 19918, May 13, 1985]

### § 440.5 Ampicillin.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Ampicillin is 6-[D-$_a$-aminobenzyl] penicillin. It is a white powder. It is so purified and dried that:

(i) It contains not less than 900 micrograms and not more than 1,050 micrograms of ampicillin per milligram on an anhydrous basis.

(ii) [Reserved]

(iii) Its loss on drying is not more than 2.0 percent.

(iv) Its pH in an aqueous solution containing 10 milligrams per milliliter is not less than 3.5 and not more than 6.0.

(v) Its ampicillin content is not less than 90 percent on an anhydrous basis.

(vi) The acid-base titration concordance is such that the difference between the percent ampicillin content when determined by nonaqueous acid titration and by nonaqueous base titration is not more than six. The potency-acid titration concordance is such that the difference between the potency value divided by 10 and the percent ampicillin content of the sample determined by the nonaqueous acid titration is not more than six. The potency-base titration concordance is such that the difference between the potency value divided by 10 and the percent ampicillin content of the sample determined by the nonaqueous base titration is not more than six.

(vii) It is crystalline.

(viii) It gives a positive identity test for ampicillin.

(2) *Labeling.* In addition to the labeling requirements prescribed by §432.5(b) of this chapter, each package shall bear on its outside wrapper or container and the immediate container the following statement, ''For use in the manufacture of nonparenteral drugs only''.

(3) *Requests for certification; samples.* In addition to complying with the requirements of §431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, loss on drying, pH, ampicillin content, concordance, crystallinity, and identity.

(ii) Samples required: 10 packages, each containing approximately 300 milligrams.

(b) *Tests and methods of assay*—(1) *Potency.* Assay for potency by any of the following methods; however, the results obtained from the microbiological agar diffusion assay shall be conclusive.

(i) *Microbiological agar diffusion assay.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed portion of the sample in sufficient sterile distilled water to give a stock solution containing 0.1 milligram of ampicillin per milliliter (estimated). Further dilute an aliquot of the stock solution with 0.1*M* potassium phosphate buffer, pH 8.0 (solution 3), to the reference concentration of 0.1 microgram of ampicillin per milliliter (estimated).

(ii) *Iodometric assay.* Proceed as directed in § 436.204 of this chapter, except in paragraph (d) of that section, add 3 drops of 1.2*N* hydrochloric acid to both the sample and working standard solutions after the addition of 0.01*N* iodine solution.

(iii) *Hydroxylamine colorimetric assay.* Proceed as directed in § 436.205 of this chapter.

(2) [Reserved]

(3) *Loss on drying.* Proceed as directed in § 436.200(a) of this chapter.

(4) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 10 milligrams per milliliter.

(5) *Ampicillin content.* Proceed as directed in § 436.213 of this chapter, using both the titration procedures described in paragraphs (e) (1) and (2) of that section. Calculate the percent ampicillin content as follows:

(i) *Acid titration.*

$$\text{Percent ampicillin content} = \frac{\dfrac{(A-B)(\text{normality of lithium methoxide reagent})}{(349.4)(100)(100)}}{(\text{Weight of sample in milligrams})(100-m)}$$

where:
A=Milliliters of lithium methoxide reagent used in titrating the sample;
B=Milliliters of lithium methoxide reagent used in titrating the blank;
*m*=Percent moisture content of the sample.

Calculate the difference between the potency and the ampicillin content as follows:

$$\text{Difference} = \frac{\dfrac{\text{Potency in micrograms per milligram}}{10}} - \text{percent ampicillin content}$$

(ii) *Base titration.*

$$\text{Percent ampicillin content} = \frac{\dfrac{(A-B)(\text{normality of perchloric acid reagent})}{(349.4)(100)}}{(\text{Weight of sample in milligrams})(100-m)}$$

where:
A=Milliliters of perchloric acid reagent used in titrating the samples;
B=Milliliters of perchloric acid reagent used in titrating the blank;
*m*=Percent moisture content of the sample.

Calculate the difference between the potency and the ampicillin content as follows:

$$\text{Difference} = \frac{\dfrac{\text{Potency in micrograms per milligram}}{10}} - \text{percent ampicillin content}$$

(6) *Crystallinity.* Proceed as directed in § 436.203(a) of this chapter.

(7) *Identity.* Proceed as directed in § 436.211 of this chapter, using a 0.5 percent potassium bromide disc, prepared as described in paragraph (b)(1) of that section.

## § 440.7  Ampicillin trihydrate.

(a) *Requirements for certification—*(1) *Standards of identity, strength, quality, and purity.* Ampicillin trihydrate is the trihydrate form of D(−)$_a$-amino-benzyl